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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/052,961 | 01/18/2002 | Joseph R. Berger | 44657-AAA-PCT-US/JPW | 3958 |

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| EXAMINER | |
|---|---|
| WANG, SHENGJUN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1617 | |

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| 08/04/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/052,961 | BERGER, JOSEPH R. | |
| | Examiner | Art Unit | |
| | Shengjun Wang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *88-106* is/are pending in the application.

4a) Of the above claim(s) *106* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88-105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 11, 2009 has been entered.

2. Newly submitted claim 106 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

3. Inventions of claims 88-105 and invention of claim 106 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the product as claimed can be used in a materially different process of using that product, such as treating alcoholic hepatitis.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 106 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### *Claim Rejections 35 U.S.C. 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 89-105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims are drawn to a unit dosage form, tablet, comprising 10 mg of oxandrolone, corn starch, hydrous lactose, hydroxypropyl methylcellulose, and magnesium stearate. The application have single example of tablet which is composed of 2.5 mg of oxandrolone, and specific amount of corn starch, hydrous lactose, hydroxypropyl methylcellulose, and magnesium stearate (page 7). The application merely mentions 10-milligram dosage, but does not disclose any further information as to the carrier and particular forms (page 4, the first paragraph). Therefore, the application as originally filed, lack support of a unit dosage form, or tablet comprising 10 mg of oxandrolone, and one of more of corn starch, hydrous lactose, hydroxypropyl methylcellulose, and stearate, nor to the particular amounts of the carriers.

### *Claim Rejections 35 U.S.C. 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 88-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metcalf et al. (of record), in view of ANAVAR® (of record, provided by applicant in IDS filed October 13, 2005), and Babu et al. (US 5,073,380) and in further view of applicants' admission at page 7.

Metcalf teach a method of using oxandrolone for nitrogen retention wherein the daily of amounts of oxandrolone are from 5 mg, 10 mg, 20 mg, and up to 150 mg. Oxandrolone were taken as single dosage daily. See, particularly, Method at page 60. Metcalf also teach that the optima dosage is about 25 mg or 30 mg a day.

Metcalf et al. do not teaches expressly a dosage forms comprising 10 mg of oxandrolone and the particular pharmaceutical excipients herein.

However, Anavar® disclosed an oxandrolone tablet, wherein the inactive ingredients include corn starch, lactose, magnesium stearate and methylcellulose. Anavar® further reveals that daily dosage of oxandrolone may be up to 20 mg/day. See the entire document. Babu et al. disclosed that hydroxypropyl methylcellulose is a typical excipient for tablet formulation. See, column 2, lines 6-8. Further, applicants admitted that tablet formulation comprising oxandrolone, corn starch, hydrous lactose, hydroxypropyl methylcellulose and magnesium stearate is known in the art. See, page 7.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art, at the time the claimed invention was made, to make a dosage composition comprising 10 mg of oxandrolone, and the particular excipients herein as the excipients herein are well-known pharmaceutical excipients and are particularly known to be useful in solid dosage forms with oxandrolone.

The 10 mg dosage would have been obvious in view the fact that it has been used in the amount of 10 mg, 20 mg, and up to 150 mg daily. One of ordinary skill in the art would have been motivated to make a tablet with 10 mg of oxandrolone for those uses more than 10 mg a day.

As to the intended use recited in the claims (for daily dosage, or not), note it is well settled that the "intended use" of a product or composition will not further limit claims drawn to a product or composition. See, e.g., In re Hack 114 USPQ 161.

***Response to the Arguments***

Applicants' remarks submitted May 11, 2009 have been fully considered, but are not persuasive.

7. With regard to the new matter rejection, the examiner maintains that a broad and general disclosure of a genus would not support a species encompassed by the genus. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967). Also see MPEP 2163.05. Applicants detailed discussion of the issues in Fujikawa v. Wattanasin, and In re Ruschig, have been considered, but are found not probative. The actual subject matters in these cases are different from those claimed herein, but the principle is the same, i.e., a description for a broad genus may not support for a particular species encompassed by the genus. In instant case, the application provides pertinent descriptions as following:

[0016] For purposes of administration in accordance with this invention, the active ingredient oxandrolone is combined with solid or liquid pharmaceutical carriers and formulated in unit dosage form using pharmacologically acceptable excipients, or dissolved or suspended in physiologically acceptable solvents or liquid vehicles for oral, percutaneous, or topical administration.

[0017] The overall daily dose of oxandrolone to provide a therapeutically effective amount in accordance with the method of this invention can ***be as low as about 2.5 milligrams and as high as about 20 milligrams,*** depending upon the patient's response and the mode of administration.

[0018] The amount of the active ingredient within the aforementioned ranges that is to be administered depends upon the age, weight and condition of the patient, as well as on factors such as the frequency and route of administration. In formulating oxandrolone, it is recognized that there may be differences between the immediate and the long term response. To account for these changes, the specific dosage given to a particular patient is based also on the individual patient's response. ***Preferably, oxandrolone is orally administered to the patient daily for a time period in the range of about 2 weeks to about 6 months.***

[0019] Attenuation of the rate of muscle mass loss in a patient can be ascertained by comparing the patient's rate of weight loss before oxandrolone therapy with that after the administration of oxandrolone has been commenced. Alternatively, or in addition, the patient's urinary nitrogen level can be monitored, a well-known expedient. A decrease in the patient's urinary nitrogen level is indicative of a decrease in muscle mass loss.

[0020] Similarly, the maintenance of a relatively stable patient's total body potassium level, as well as an increase in the patient's total body potassium level, upon oxandrolone administration indicates that a therapeutically effective amount of oxandrolone is being administered. A patient's total body potassium level can be monitored, for example, as described in Kotler et al., The American Journal of Clinical Nutrition, 42:1255-1265 (December 1985) and Pierson, Jr., et al., Am. J. Physiol., 246 (Renal Fluid Electrolyte Physiol. 21):F234-F239 (1984).

[0021] The route of administration can be oral, percutaneous, transdermal, sublingual, buccal, intravenous, intramuscular, or the like. ***Of these, oral administration is preferred. The patient's daily dose of the active ingredient preferably is in the range of about 7.5 milligrams, but may exceed 20 milligrams based on clinical response. This daily dose can be given in tablet form as a single dose, or as plural divided doses, preferably 2 to 3 divided doses.*** The requisite daily dose can also be supplied continuously, for example, by a transdermal patch worn by the patient or intravenously. ***If the oxandrolone is administered orally, dosages in the range of about 2 to about 5 milligrams three to four times daily typically may be utilized.***

[0022] Oxandrolone tablets are manufactured using standard solid dose form technology in accordance with United States Pharmacopeia (USP) specifications (see, for example, The United States Pharmacopeia, 22nd Revision, pp. 981-982). Specifically, a typical 150-milligram tablet contains the following:

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  Oxandrolone, USP  2.5 mg
  Corn Starch, NF  30.0
 mg
  Lactose NF (hydrous) 113.0 mg
  Hydroxypropyl
 Methylcellulose, USP  3.0 mg
  Magnesium Stearate  1.5 mg
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150.0 mg

[0023] The terms "unit dosage form" and "unit dose" as used in the present specification and claims refer to a physically discrete unit or units suitable as unitary doses for patients, each unit containing a predetermined quantity of the active ingredient calculated to produce the desired therapeutic effect in association with the pharmacologically acceptable carrier. The specifications for the unit dosage forms of this invention are dictated in part and are also dependent upon (a) the unique characteristics of the active ingredient and (b) the particular therapeutic effect to be achieved, as well as upon limitations inherent in the art of compounding such active ingredient for the therapeutic use disclosed in detail in this specification. Examples of suitable unit dosage forms in accordance with this invention are tablets, pills, powder packets, wafers, cachets, segregated multiples of any of the foregoing, transdermal patches, aliquots of injectables, and the like forms. (page 5, line 27 to page 8, line 4, emphasis added)

8. It is noted that the application mentioned 2.5 mg to 20 mg daily dosage, wherein the daily dosage may be give in tablet form as a single dose, but preferably 2-3 divided doses. It is particularly state: ***"If the oxandrolone is administered orally, dosages in the range of about 2 to about 5 milligrams three to four times daily typically may be utilized."*** Reading those description, one of ordinary skill in the art would not be reasonably convey that at the time of the invention was made, applicant has possession of the 10 mg tablet as herein claimed, as the disclosure provide merely a broad range of 2.5 to 20 mg daily dosage, which may be divided into several doses. It is much broader with respect to the carrier and excipients.

9. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986), particularly, the cited reference as a whole, teach that the daily dosage of oxandrolone may in 10 mg , 20 mg, 30 mg, or more, the references never require that oxandrolone be administered in a single dosages. There fore , it

would have been obvious to make a unite dose contain 10 mg oxandrolone, either for those who take 10 mg daily, or for those who take divided doses. The 132 declaration have been fully considered, but are not persuasive for reasons as discussed in the prior office action. Particularly, the "pill-burden" issues are not sufficient to rebut the prima facie case of obviousness, as a merely change of size, shape of a subject matter would not make the subject matter patentably distinguish. In re Rose, 220 F.2d 459, 105 USPQ 237 (CCPA 1955); In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). Further, it is well settled that "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617

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